Accelerated Hypofractionation, **C**hemotherapy, **I**ntensity **M**odulation and **E**valuation of **D**ose **E**scalation in **O**ro**p**haryngeal Cancer (ArChIMEDEs-Op)

Trial Design

Single-centre, single-arm, feasibility study

Objective

To determine whether it is safe and feasible to deliver a 5 week schedule of dose escalated intensity modulated chemoradiotherapy for poor prognosis patients with locally advanced squamous carcinoma of the oropharynx (SCCOP) in the context of a feasibility study

Outcome Measures

Primary:

- Full radiotherapy has been received as planned and the absence of consequential damage: defined by the absence of Grade 3 mucositis at 3 months

Secondary:

- Duration of Grade 3 mucositis: defined as the number of days of Grade 3 mucositis according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 3
- Incidence of acute Grade 4 toxicity defined according to the NCI CTCAE version 4
- Incidence of ≥ Grade 3 late toxicity defined according to the Radiation Therapy Oncology Group (RTOG) and NCI CTCAE version 4 scoring systems
- Complete response rate at 3 months defined as no clinically visible (including endoscopic evaluation), palpable or measurable disease on imaging OR the absence of residual tumour on directed biopsy/neck dissection. The primary tumour and regional lymph nodes will be considered separately
- 2 year local control defined as no re-appearance of tumour within primary site (including immediately adjoining anatomical sites) or regional lymph nodes after complete response
- 2 year disease free survival defined in whole days, as the time from entry into the study until disease recurrence or death from any cause, whichever is first. Patients will be censored at the date last seen alive and relapse free. All patients will be followed up for at least 5-years
- 2 year overall survival defined in whole days as the time from entry into the study until death from any cause. Patients will be censored at the date last seen alive. All patients will be followed up for at least 5-years
- Incidence of feeding tube dependency at one year defined by the patient requiring supplementation of nutrition by a feeding tube

Patient Population

Patients with HPV and P16 negative locally advanced squamous carcinoma of the oropharynx or patients with P16 positive tumours if stage N2b-3 and greater than 10 pack year history of smoking

Sample Size

15 patients

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Histologically proven, P16 negative SCCOP deemed suitable for radical primary chemoradiotherapy with curative intent requiring bilateral neck irradiation or patients with P16 positive tumours if stage N2b-3 and greater than 10 pack year history of smoking. Neoadjuvant chemotherapy and pre or post chemoradiation neck dissections are permitted
2. Only patients requiring bilateral radiotherapy
3. Age ≥18 and <75 years
4. World Health Organisation (WHO) performance status 0 or 1
5. Adequate bone marrow: absolute neutrophil count > 1,800 cells/mm^3, platelets > 100,000 cells/mm^3, haemoglobin > 8.0 g/dl
6. Creatinine clearance > 50 ml/minute
7. Informed consent

Exclusion Critera:

1. Prior invasive malignancy (except basal cell carcinoma and cervical intraepithelial neoplasia) within last 3 years
2. Prior radiotherapy to the head and neck region
3. Pregnancy and/or lactation
4. Reproductive capability and dis-agreement to use contraceptive
5. Contraindications to cisplatin and carboplatin chemotherapy including active vascular disease (e.g. myocardial within last 6 months, angina and symptomatic peripheral vascular disease)
6. Non curative intent
7. Non squamous cell carcinoma histology
8. Nasophaynx, larynx, hypopharynx, salivary gland or sino-nasal primary site
9. Other physical or psychiatric disorder that may interfere with subject compliance, adequate informed consent, follow up or determine the causality of adverse events
10. Suitable for unilateral radiotherapy

Trial Schema